REMARKS

Claims 58-67 are pending. No claims have been added, canceled or amended herein. Accordingly, claims 58-67 will remain pending and under examination upon consideration of this Communication.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the February 24, 2004 Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The Claimed Invention

The instant invention provides methods and reagents for predicting pregnancy outcome. This invention is based upon the surprising discovery of a correlation between pregnancy outcome and urinary levels of the early pregnancy-associated molecular isoform of hCG. Methods and reagents are provided for the determination of this analyte in a sample.

Double Patenting Rejection

The Examiner rejected claims 58-67 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53, 59, 60, 65, 71, 72, and 77-82 of U.S. Serial No. 09/017,976, now U.S. Patent No. 6,500,627, for the reasons of record.

In response, applicants will submit a terminal disclaimer at such time as the instant claims are deemed otherwise allowable.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claim 62 under 35 U.S.C. §103(a) as allegedly unpatentable over Penfold et al. (1997) in view of Morton et al. (1988).

In response, applicants respectfully traverse, for the reasons of record stated in applicants' September 16, 2002 Amendment and for the additional reasons set forth below.

Claim 62 provides a method for determining the amount of an early pregnancy-associated molecular isoform of hCG (EPMI-hCG) present in a sample.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, that the cited references, when combined, teach or suggest every element of the claim. Second, that one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, that there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that the cited references fail to support a *prima facie* case of obviousness because they do not teach or suggest every element of the claimed invention. That is, the cited references fail to teach or suggest methods for determining the early pregnancy-associated molecular isoform of hCG ("EPMI-hCG") in a sample.

Penfold teaches an immunoassay for the detection of urinary analytes, including hCG. Penfold does not teach EPMI-hCG or its detection.

Morton teaches monoclonal antibodies for the detection of an early pregnancy factor ("EPF"). Morton does not teach the EPMI-hCG of the instant claims.

The Examiner alleges that it would have been obvious to substitute the antibodies in the immunoassay taught by Penfold with the monoclonal anti-EPF antibodies of Morton to determine the amount of EPMI-hCG present in a sample.

Applicants respectfully disagree. EPF is known in the art to be a heat shock protein (see Exhibit A of applicants' September 16, 2002 Amendment). EPMI-hCG is not a heat shock protein. Instead, it is a chorionic gonadotropin (see p. 2, lines 11-12, and p. 24, lines 2-6, of the specification). Due to the specificity of monoclonal antibodies, one of skill would not expect that a monoclonal antibody that detects a heat shock protein would also detect a chorionic gonadotropin. Accordingly, applicants maintain that one of skill would have no reasonable expectation of success in using the anti-EPF antibodies of Morton in the immunoassay of Penfold to detect EPMI-hCG.

The Examiner further asserts that it is proper for the purposes of this rejection to interpret "early pregnancy associated molecular isoform of hCG" as any "early pregnancy factor or EPF" absent a definitive and distinctive characterization of this hCG isoform. To support this assertion, the Examiner relies on the rule that claims are given their broadest possible interpretation consistent with the specification.

In response, applicants maintain that the Examiner has given the term "EPMI-hCG" an interpretation broader than, and

inconsistent with, the meaning supported by the instant specification. The specification, at page 24, lines 2-6, teaches that the present immunoassays were designed "to measure unique early pregnancy associated molecular isoforms (EPMI) of hCG. These isoforms, likely to differ by carbohydrate composition, are predictive of a successful pregnancy outcome." The term "hCG" is defined at page 2, lines 11-12, as "human chorionic gonadotropin." Thus, the term "EPMI-hCG" can not be construed to encompass any and all early pregnancy factors as the Examiner asserts at pages 3-4 of the Office Action. To the contrary, the term EPMI-hCG can only encompass proteins that are molecular isoforms of hCG. Any protein that is not a molecular isoform of hCG cannot be an "EPMI-hCG." Applicants reiterate that the Examiner has set forth no evidence that the EPF taught by Morton is a molecular isoform of hCG, or even a gonadotropin. Instead, it is a heat shock protein, as taught by Morton (1998), of record. Applicants thus maintain that the early pregnancy associated isoform of hCG recited in the instant claims does not include heat shock proteins, and specifically, does not include the EPF of Morton.

Thus, the cited references fail to teach all elements of the claimed method, in that they fail, inter alia, to teach the detection of an early pregnancy-associated molecular isoform of hCG. It follows that the cited references also do not create a motive to combine or a reasonable expectation of success. Accordingly, the Examiner has failed to set forth a *prima facie* case of obviousness over Penfold and Morton.

The Examiner also rejected claims 58-61, 63, and 65-67 under 35 U.S.C. §103(a) as allegedly unpatentable over Penfold, Morton, and further in view of Birken et al. (1993).

In response to the Examiner's rejection, applicants respectfully traverse, for the reasons of record stated in applicants' September 16, 2002 Amendment and for the additional reasons set forth below.

Claims 58-61 provide a method for predicting pregnancy outcome in a subject. Claims 63 and 65-67 provide a diagnostic kit for predicting pregnancy outcome in a subject.

Penfold and Morton are described above. Birken teaches an analytical method for separating intact hCG from nicked hCG and the hCGβ core fragment using column fractionation. Birken also teaches antibodies B108 and B109 which recognize intact hCG.

Applicants maintain that Birken fails to overcome the deficiency of Penfold and Morton recited above. In particular, Birken does not teach or suggest EPMI-hCG, or a method for its detection. Moreover, none of the cited references teaches or suggests the element of a *ratio* of EPMI-hCG to intact hCG, as recited in part (c) of claim 58. Thus, the cited references do not teach every element of the rejected claims and therefore the Examiner has failed to establish a *prima facie* case of obviousness.

In view of the above remarks, applicants maintain that claims 58-67 satisfy the requirements of 35 U.S.C. §103(a).

Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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